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Exercise and Monitoring of Central Aortic Pressure

Background

Exercise is universally recommended in healthy individuals, people with cardiovascular disease risk factors, and for those who have known cardiovascular disease. Improving exercise endurance has been shown to reduce cardiovascular risk factors (weight, blood glucose), improve cardiovascular health, improve cognitive function, and reduce mortality.[1-4] However, the performance of exercise (i.e., during the period of exercise) can have adverse health consequences related to the stress placed on the cardiovascular system. Standard vital signs monitoring alone (i.e., heart rate, brachial BP) may not adequately indicate and track the direct physiologic benefits as well as adverse effects associated with exercise training both acutely and over the long-term.

Non-Invasive Assessment of Central Aortic Pressure

Central aortic pressure measurement based on pulse wave analysis (PWA) provides a number of digital vascular biomarkers (e.g., central aortic systolic and diastolic pressures, central pulse pressure, augmentation pressure, augmentation index, subendocardial viability ratio) that are used for identification and monitoring of elevated BP and associated risks. PWA is an approach that has been proposed broadly and may have applicability to exercise related vascular changes.

Management of hypertension through cuff measurement of peripheral (brachial artery) pressures, has dramatically but incompletely improved the ability of health care providers and their patients to control hypertension and reduce associated end-organ damage. Multiple issues likely contribute to the ongoing socioeconomic burden of hypertension despite the availability of multiple effective medications and widespread educational efforts. Such issues include, but are not limited to, case finding (early diagnosis), continuity and continued follow-up of care, affordability of care, medication adverse effects, medication compliance and challenges in modifying lifestyle behavior.

An underappreciated but clinically relevant area to consider is the precision and reliability of current monitoring, which is based on brachial BP measurements, including patient and health care provider factors. In general, cuff brachial BP might be viewed as a surrogate for central (i.e., aortic) blood pressures; however, differences exist between brachial and aortic BPs and the differences can vary among different individuals. Aortic pressure represents the actual pressure that is transmitted to organs affected by hypertension (e.g., heart, brain, kidney) due to the closer proximity of the ascending aorta to these vital organs. Non-invasive pulse wave analysis (PWA) is a technique that is based on transformation of peripheral (brachial) arterial pressure waveforms into central aortic pressures waveforms. A key principle is the understanding that the measured peripheral brachial pressure is a combination of the forward systolic pressure wave and the pressures waves reflected back from various arterial branching points. PWA allows for discrimination of the various pressure wave features. The following parameters are obtained from PWA:

- Central aortic systolic and diastolic BPs
- Augmentation index (AIx, a ratio expressing or the reflected pressure wave and pulse pressure in the central aorta). An increase in AIx is an indicator of arterial stiffness.
- Augmentation pressure (AP, the added pressure from the reflected wave). An increase in AP is an indicator of arterial stiffness)
- Central aortic pulse pressure (central systolic minus diastolic BP).
- Pulse pressure amplification (the ratio of peripheral to central pulse pressure)

Central pressure variables derived from PWA are used to complement peripheral (brachial) BPs; however, significant variability exists such that central BPs cannot be reliably inferred from brachial pressures. The ability to obtain and quantify these variables provide in-depth understanding of the vascular physiology and help determine risk and potential treatment strategies.

The technology for non-invasive assessment of central aortic pressures through PWA is currently available and cleared by the United States Food and Drug Administration (FDA). In recognition of the clinical utility of PWA, a Current Procedural Terminology (CPT) code has been established. The SphygmoCor® XCEL system is a dual arterial pressure monitoring medical device measuring both brachial BPs and central aortic pressures (using partial cuff inflation to record the outgoing brachial waveform), which can be obtained in the clinic at the same time. The SphygmoCor XCEL is the only FDA cleared medical device for non-invasive central arterial pressure waveform measurement and analysis for all adults. The incorporation of PWA in the SphygmoCor System was developed to help guide treatment decisions designed to prevent or reduce long-term target organ damage and cardiovascular events resulting from increased aortic pressure. The PULSE® dual arterial monitoring system represents the latest and most advanced generation of devices based on the SphygmoCor technology and is specifically designed for both home and clinic use.

The SphygmoCor XCEL and PULSE systems are dual arterial pressure monitoring medical device for the measurement of brachial and central aortic pressures, which can be obtained at the same time.

Non-invasive monitoring of vascular biomarkers derived from pulse wave analysis such as central aortic blood pressure (BP), which differ significantly from the peripheral brachial BP, can be clinically useful for assessing the safety of exercise, quantifying the benefits of exercise, and for proactively optimizing exercise prescriptions, particularly for those with cardiovascular disease. While not widely recognized, such monitoring can be useful in healthy individuals participating in recreational or competitive training. Increasingly, peer-reviewed publications indicate that integrating non-invasively obtained central aortic pressure waveform with cardiovascular related features provides additional and independent information on cardiovascular health including the safety and benefits of exercise training.

Exercise and Blood Pressure Changes

Several examples supporting the utility of PWA for exercise monitoring can be found in publications dating back more than a decade. A study by Coates et al suggests that over-training in the short-term is associated with increased arterial stiffness (as measured by pulse wave velocity (PWV)), which may have an adverse effect on training goals (and possibly long-term vascular health).[5] Other investigators have also demonstrated that overtraining is associated with reduced exercise performance, reduced exercise heart rate, reduced stroke volume, and reduced cardiac output.[6-10] These reports have vascular health implications for recreational and professional athletes. Dual arterial blood pressure (BP) monitoring (i.e., central aortic pressure variables and peripheral (brachial) BP) allows for a comprehensive assessment and can be useful in determining optimal exercise programs (intensity, duration) above that provided by brachial BP alone.

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Denham et al documented that a reduction in augmentation index (AIx) was statistically associated with increases in maximum oxygen consumption during peak exercise (VO_2peak).[11] In other words, reduced risk of cardiovascular disease as demonstrated by reduced AIx was associated with improved exercise aerobic capacity and that one could consider AIx as a surrogate marker of the adequacy of exercise training (or of improved VO_2peak).

A basic question relates to whether the measures of brachial and aortic pressures are redundant to our understanding of exercise physiology in the presence of underlying vascular abnormalities. The previous reports are consistent with the premise. A direct evaluation was published by Millen and colleagues who studied post-exercise effects on central pressure variables derived from PWA and on brachial BP in 20 pre-hypertensives and hypertensive adults.12 The findings were that 15 minutes after aerobic exercise, aortic reflected wave pressures decrease (AIx decreased from 26.3 to 7.8%, p<0.001) and that this contributed toward decreases in central aortic BP (132 to 122 mmHg, p<0.001) and that such changes did not occur in brachial systolic pressure (141 to 139 mmHg, p=0.55). While the long-term clinical impact has not been evaluated, the study highlights that physiologic differences can occur between central and brachial pressures during exercise.

Findings in publications seem to differ in the direction of changes with brachial and central pressures associated with exercise.[13,14] However, it is difficult to compare various studies due to differences in methodology (e.g., short-term training vs. longer term training, incorporation of ultra-endurance athletes vs. those with regular fitness programs, types of training, duration of training, cross-sectional vs. prospective studies). Nevertheless, what is apparent is that changes (or lack of changes) in brachial BP can be different from those observed with central pressure parameters. Knez et al evaluated hemodynamics using PWA in ultra-endurance male athletes (n=36) and matched controls (n=44).[13] While no significant differences between groups in AIx, brachial or central pulse systolic or pulse pressure were observed, two potentially important findings were documented. First, athletes had significantly increased subendocardial viability ratio (226 ± 42% versus 198 ± 46%; P < 0.001), an indicator of myocardial perfusion that is obtained from central aortic PWA and not from brachial blood pressure. Second, the amount of exercise training volume was significantly associated with central pulse pressure (r = –0.46; p=0.002), but not brachial pulse pressure (r = –0.28; p>0.05). The study shows that central and brachial pulse pressures are differentially affected by exercise, with central but not brachial pulse pressure being significantly related to the amount of time spent in aerobic activity.[13]

In a study of ultra-endurance athletes, central and brachial pulse pressures were differentially affected by exercise, with central but not brachial pulse pressure being significantly related to duration of aerobic activity.

Tomoto et al evaluated PWA in 36 trained high performance endurance runners in order to determine the effect of short-term intense endurance training on aortic blood pressure.[14] Testing was performed before and after a 7-day training camp. Training included sprinting and long distance running to achieve of target of 26 km daily. The population was segmented into two groups, which was determined by whether or not the target training was achieved. Aortic systolic BP and tension time index (surrogate for myocardial oxygen demand) were significantly elevated after the camp in the group reaching the target but not in the other group (target not reached). However, both groups did not exhibit alterations in brachial BP. Significant correlations were documented between daily training distance and changes in aortic systolic BP ($r = 0.61$, $p<0.001$) and pulse pressure ($r = 0.42$, $p = 0.016$). These results are consistent with other publications indicating differences in changes between brachial and aortic BP associated with exercise. The data appears to indicate that monitoring of brachial and central pressures variables is not redundant. In other words, a full understanding related to exercise should include both measures as obtained in a single dual arterial blood pressure monitoring system. Such observations should be considered when determining physiological effects of exercise training and monitoring during exercise training programs.

A meta-analysis was published Ashor and colleagues in 2014 with the objective of evaluating the effects of different exercise modalities (aerobic, resistance or combined) on arterial stiffness (as assessed by pulse wave velocity (PWV) and AIx).[15] Forty-two studies involving 1,627 participants were included in this analysis. Aerobic exercise improved both PWV and AIx. The authors concluded that aerobic exercise training improved arterial stiffness significantly and that the effect was enhanced with higher aerobic exercise intensity and in participants with greater arterial stiffness at baseline.

Aerobic exercise training has been shown to improve arterial stiffness in a meta-analysis of 42 studies.

In summary, including central aortic pressure and its cardiovascular parameters using dual arterial BP monitoring as obtained through SphygmoCor technology enables a more comprehensive clinically relevant assessment for (a) quantifying the benefits of exercise, (b) the safety of exercise training programs, and (c) proactively optimizing exercise prescriptions (e.g., intensity, duration), relative to brachial BP monitoring alone.

Professional Sports and Elevated Blood Pressure

A relevant aspect of exercise relates to professional sports such as football and basketball where body size (height, weight) and strength represent the extreme of the general population. These high performance athletes commit their lives to obtaining optimal physical attributes for their specific sports. However, the diet, supplements and training associated with their chosen profession may have adverse consequences that should be considered for regular vascular monitoring in order to maintain a quality and quantity of life long after their sports careers have ended. Publications are available for National Football League players. These reports indicate that such athletes, specifically those who have a higher body mass index and participate as linemen, have an increased prevalence of hypertension and mortality from cardiovascular disease.[16-22] The key issues then relate to early identification of risk and intervention in the hopes of diminishing the development of cardiovascular disease.

Perhaps the most comprehensive publication relevant to risks for cardiovascular disease is from Tucker and colleagues.[17] The investigators evaluated risk factors for cardiovascular disease (CVD) in 504 active National Football League (NFL) players and to compare the data to that obtained in the Coronary Artery Risk Development in Young Adults (CARDIA) study (a population-based observational study of 1,959 participants aged 23 to 35 years). The NFL players compared with the CARDIA group had higher body mass index (31.4 vs. 25.9 kg/m^2, p<0.001), had lower reported smoking (0.1% vs. 30.5%, p<0.001) and were less likely to have impaired fasting glucose (6.7% vs. 15.5%, p<0.001). No differences in lipid levels were observed. NFL players had a higher prevalence of hypertension (13.8% vs. 5.5% p<0.001) and prehypertension (64.5% vs. 24.2%, p<0.001), both of which were associated with elevated body mass index. Of note, hypertension prevalence was similar across race. In summary, despite several cardiovascular risk factors that were lower in NFL players relative to healthy young-adult men, the NFL players had a higher prevalence of hypertension, which given their relatively young age has clinically significant implications for their long-term cardiovascular health.

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Based on the above, the obvious question is how early can risks of cardiovascular disease be detected in these athletes. An important study that addresses the question was performed by Kim and colleagues who evaluated Collegiate US football athletes through 3 complete years of football training.[21] Subject evaluation included echocardiography and assessment of arterial stiffness by pulse wave velocity (PWV). Demographics of the 126 subjects included were: white 49%, black 50%, non-linemen 61%; linemen 39%, weight 101.1 (21.0) kg, mean systolic blood pressure of 129.1 (11.6) mm Hg at baseline of the freshman season. Subjects experienced weight gain (mean [SE], 4.74 [0.6] kg; p<0.001), increased systolic BP (mean [SE], 11.6 [1.6] mm Hg; p<0.001), and increased PWV (mean [SE], 0.24 [0.09] m/s; p=0.007) over 3 years (adjusted for race, height, and player position). Increase PWV indicated increased arterial stiffness. Weight gain was associated with increased PWV (p=0.003) and left ventricular hypertrophy (odds ratio, 1.09 [95% CI,1.05-1.14]; p<0.001). Increased systolic blood pressure was associated with PWV (p=0.007) and the development of left ventricular hypertrophy (odds ratio, 1.04 [95% CI, 1.01-1.07]; p=o.02). In summary, collegiate football athletes who gain weight and develop increased systolic blood pressure are at risk for left ventricular hypertrophy and arterial stiffening consistent with the development of clinically relevant changes occurring early in an athlete's career and reasonably can be expected to worsen without identification and management.

The above clinical research was substantiated further in a prospective, longitudinal study recording BP, the incidence of hypertension, and left ventricular remodeling among 113 collegiate football players.[22] Participation in football was associated with increases in systolic BP (116±8 vs. 125±13 mm Hg; p<0.001) and diastolic BP (64±8 mm Hg vs. 66±10 mm Hg; p<0.001). At the postseason assessment, the majority of athletes met criteria for prehypertension (47%) or stage 1 hypertension (14%). Lineman field position, intra-season weight gain, and family history of hypertension were the strongest independent predictors of postseason BP. Among linemen, there was a significant increase in the prevalence of concentric left ventricular hypertrophy (3% vs. 31%; p<0.001). The authors concluded that "Enhanced surveillance and carefully selected interventions may represent important opportunities to improve later-life cardiovascular health outcomes in this population."[22]

Enhanced surveillance and carefully selected interventions may represent important opportunities to improve later-life cardiovascular health outcomes in collegiate football players.

In summary, published research has identified that athletes (collegiate and professional) who have large body sizes that are suited for specific sports such as football have an increased risk of elevated blood pressure, heart changes (left ventricular hypertrophy) associated with elevated blood pressure, and possibly increased arterial stiffness. These documented vascular abnormalities are occurring at a young age and therefore have significant implications for long-term cardiovascular health.

Considerations for Incorporating Central Aortic Pressure Monitoring as Part of Exercise Programs

Monitoring of central aortic pressure (i.e., frequency, number and type of variables, target values) should be personalized to the individual based on their health status and their performance targets as described in the following two tables. The exercise program based on the blood pressure (both peripheral and central) evaluation can inform the decisions to alter the intensity and/or frequency of the exercise program, or potentially change the components of the exercise intervention.

TABLE 1: Exercise Populations and Health Status

Healthy - Recreational athletics
Healthy - Ultra-endurance athletics
Healthy - Professional/collegiate athletics
At-risk of cardiovascular disease
Known cardiovascular disease or disease that effects the cardiovascular system

TABLE 2: Utility of Central Aortic Pressure Monitoring in the Performance of Exercise Programs

Cardiovascular risk assessment prior to an exercise training program
Monitoring of cardiovascular effects (positive and negative) during exercise training
Assessment of the cardiovascular effects of an exercise training program
Evaluation and monitoring of cardiovascular safety in people with diseases known to have adverse effects on the cardiovascular system
Optimizing training intensity based on cardiovascular physiology

Clinical examples for interpreting the results from pulse wave analysis are listed below. As with any clinical situation, patients should consult with their health care providers.

- Increased central systolic or diastolic pressure: hypertension.
- Increased central pulse pressure: indicative of hypertension and possibly increase aortic stiffness.

- Increased augmentation pressure and augmentation index: likely increased aortic stiffness.
- Decreased subendocardial viability ratio: indicative of decreased oxygen supply to inner cardiac muscle relative to demand, which becomes clinically relevant in the setting of underlying cardiac disease.
- The opposite direction for the above examples can be considered as more desirable outcomes. Exercise, when appropriately administered, is expected to positively impact the aforementioned variables.

Conclusions

Based on the aforementioned clinical research and the availability of dual arterial monitoring systems, including central aortic pressure and its cardiovascular parameters using devices based on SphygmoCor technology (SphygmoCor XCEL, PULSE) can enable a more comprehensive clinically relevant assessment for (a) quantifying the benefits of exercise, (b) the safety of exercise training programs, and (c) proactively optimizing exercise prescriptions (e.g., intensity, duration), relative to brachial BP monitoring alone.

For collegiate and professional athletes, risk assessment and management of cardiovascular abnormalities (particularly hypertension) with home monitoring of comprehensive vascular health based on brachial and central aortic blood pressure utilizing a dual arterial blood pressure monitoring system can be an important intervention for early identification and optimization of therapies with the intention of reducing the impact of vascular disease. The proposition is relevant to participants in higher risk athletic sports and in recreational athletes who are interested in knowing more about the impact of exercise on their cardiovascular health.

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